<110> Xia, Yu-Ping et al.

<120> METHODS FOR TREATING INFLAMMATORY SKIN DISEASES

<130> REG 710b

<140> 09/773,877
<141> 2001-01-31

<160> 27

<170> PatentIn version 3.0

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gataatgccc gggccctttt catggaccct gacaaatg   38

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ttcctgggca acagctggat atctatgatt gtattggt   38

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<400> 8
attttcatgc acaatgacct cggtgctctc ccgaaatcg   39

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2

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<400> 10
gataatgccc gggccatttt catgcacaat gacctcggt   39

<210> 11
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<223> Flt1(1-3)-Fc

<220>
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<222> (1)..(1704)

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atg gtc agc tac tgg gac acc ggg gtc ctg ctg tgc gcg ctg ctc agc   48
Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
1   5   10   15

tgt ctg ctt ctc aca gga tct agt tca ggt tca aaa tta aaa gat cct   96
Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro
            20   25   30

gaa ctg agt tta aaa ggc acc cag cac atc atg caa gca ggc cag aca   144
Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
        35   40   45

ctg cat ctc caa tgc agg ggg gaa gca gcc cat aaa tgg tct ttg cct   192
Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
    50   55   60

gaa atg gtg agt aag gaa agc gaa agg ctg agc ata act aaa tct gcc   240
Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65   70   75   80

tgt gga aga aat ggc aaa caa ttc tgc agt act tta acc ttg aac aca   288
Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
                85   90   95

gct caa gca aac cac act ggc ttc tac agc tgc aaa tat cta gct gta   336
Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
            100   105   110

cct act tca aag aag aag gaa aca gaa tct gca atc tat ata ttt att   384
Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
            115   120   125

agt gat aca ggt aga cct ttc gta gag atg tac agt gaa atc ccc gaa   432
Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
        130   135   140

3

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att ata cac atg act gaa gga agg gag ctc gtc att ccc tgc cgg gtt      480
Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145             150             155                 160

acg tca cct aac atc act gtt act tta aaa aag ttt cca ctt gac act      528
Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
                165             170             175

ttg atc cct gat gga aaa cgc ata atc tgg gac agt aga aag ggc ttc      576
Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
            180             185             190

atc ata tca aat gca acg tac aaa gaa ata ggg ctt ctg acc tgt gaa      624
Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
            195             200             205

gca aca gtc aat ggg cat ttg tat aag aca aac tat ctc aca cat cga      672
Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
210             215             220

caa acc aat aca atc ata gat gtc caa ata agc aca cca cgc cca gtc      720
Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val
225             230             235             240

aaa tta ctt aga ggc cat act ctt gtc ctc aat tgt act gct acc act      768
Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr
            245             250             255

ccc ttg aac acg aga gtt caa atg acc tgg agt tac cct gat gaa aaa      816
Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys
            260             265             270

aat aag aga gct tcc gta agg cga cga att gac caa agc aat tcc cat      864
Asn Lys Arg Ala Ser Val Arg Arg Arg Ile Asp Gln Ser Asn Ser His
            275             280             285

gcc aac ata ttc tac agt gtt ctt act att gac aaa atg cag aac aaa      912
Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys
290             295             300

gac aaa gga ctt tat act tgt cgt gta agg agt gga cca tca ttc aaa      960
Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys
305             310             315             320

tct gtt aac acc tca gtg cat ata tat gat aaa gca ggc ccg ggc gag     1008
Ser Val Asn Thr Ser Val His Ile Tyr Asp Lys Ala Gly Pro Gly Glu
                325             330             335

ccc aaa tct tgt gac aaa act cac aca tgc cca ccg tgc cca gca cct     1056
Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
            340             345             350

gaa ctc ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag     1104
Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
            355             360             365

gac acc ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg     1152
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
370             375             380
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4

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gac gtg agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac          1200
Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
385                 390                 395                 400

ggc gtg gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac          1248
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
                405                 410                 415

aac agc acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac          1296
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
                420                 425                 430

tgg ctg aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc          1344
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
                435                 440                 445

cca gcc ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga          1392
Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
        450                 455                 460

gaa cca cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag          1440
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
465                 470                 475                 480

aac cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac          1488
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
                485                 490                 495

atc gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag          1536
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
                500                 505                 510

acc acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc          1584
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
                515                 520                 525

aag ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca          1632
Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
        530                 535                 540

tgc tcc gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc          1680
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
545                 550                 555                 560

ctc tcc ctg tct ccg ggt aaa tga                                          1704
Leu Ser Leu Ser Pro Gly Lys
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<210>   12
<211>   567
<212>   PRT
<213>   Artificial Sequence

<220>
<223>   Flt(1-3)-Fc

<400>   12


Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
1               5                   10                  15
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5

Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro
        20   25   30

Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
        35   40   45

Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
    50   55   60

Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65   70   75   80

Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
            85   90   95

Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
        100   105   110

Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
        115   120   125

Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
    130   135   140

Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145   150   155   160

Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
            165   170   175

Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
            180   185   190

Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
    195   200   205

Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
    210   215   220

Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val
225   230   235   240

Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr
            245   250   255

6

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Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys
        260             265             270

Asn Lys Arg Ala Ser Val Arg Arg Arg Ile Asp Gln Ser Asn Ser His
        275             280             285

Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys
    290             295             300

Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys
305             310             315             320

Ser Val Asn Thr Ser Val His Ile Tyr Asp Lys Ala Gly Pro Gly Glu
            325             330             335

Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
            340             345             350

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
        355             360             365

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
        370             375             380

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
385             390             395             400

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
            405             410             415

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
            420             425             430

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
        435             440             445

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
    450             455             460

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
465             470             475             480

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
            485             490             495
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7

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
        500   505   510

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
        515   520   525

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
    530   535   540

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
545   550   555   560

Leu Ser Leu Ser Pro Gly Lys
                565

<210>   13
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<223>   Flt1(1-3 deltaB) (Mut 1)

<220>
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<222>   (1)..(1674).

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1   5   10   15

tgt ctg ctt ctc aca gga tct agt tca ggt tca aaa tta aaa gat cct   96
Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro
            20   25   30

gaa ctg agt tta aaa ggc acc cag cac atc atg caa gca ggc cag aca   144
Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
        35   40   45

ctg cat ctc caa tgc agg ggg gaa gca gcc cat aaa tgg tct ttg cct   192
Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
    50   55   60

gaa atg gtg agt aag gaa agc gaa agg ctg agc ata act aaa tct gcc   240
Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65   70   75   80

tgt gga aga aat ggc aaa caa ttc tgc agt act tta acc ttg aac aca   288
Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
                85   90   95

gct caa gca aac cac act ggc ttc tac agc tgc aaa tat cta gct gta   336
Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
            100   105   110

8

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cct act tca aag aag aag gaa aca gaa tct gca atc tat ata ttt att      384
Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
            115                 120                 125

agt gat aca ggt aga cct ttc gta gag atg tac agt gaa atc ccc gaa      432
Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
        130                 135                 140

att ata cac atg act gaa gga agg gag ctc gtc att ccc tgc cgg gtt      480
Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145                 150                 155                 160

acg tca cct aac atc act gtt act tta aaa aag ttt cca ctt gac act      528
Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
                165                 170                 175

ttg atc cct gat gga aaa cgc ata atc tgg gac agt aga aag ggc ttc      576
Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
            180                 185                 190

atc ata tca aat gca acg tac aaa gaa ata ggg ctt ctg acc tgt gaa      624
Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
            195                 200                 205

gca aca gtc aat ggg cat ttg tat aag aca aac tat ctc aca cat cga      672
Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
    210                 215                 220

caa acc aat aca atc ata gat gtc caa ata agc aca cca cgc cca gtc      720
Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val
225                 230                 235                 240

aaa tta ctt aga ggc cat act ctt gtc ctc aat tgt act gct acc act      768
Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr
            245                 250                 255

ccc ttg aac acg aga gtt caa atg acc tgg agt tac cct gat gaa att      816
Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Ile
            260                 265                 270

gac caa agc aat tcc cat gcc aac ata ttc tac agt gtt ctt act att      864
Asp Gln Ser Asn Ser His Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile
            275                 280                 285

gac aaa atg cag aac aaa gac aaa gga ctt tat act tgt cgt gta agg      912
Asp Lys Met Gln Asn Lys Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg
        290                 295                 300

agt gga cca tca ttc aaa tct gtt aac acc tca gtg cat ata tat gat      960
Ser Gly Pro Ser Phe Lys Ser Val Asn Thr Ser Val His Ile Tyr Asp
305                 310                 315                 320

aaa gca ggc ccg ggc gag ccc aaa tct tgt gac aaa act cac aca tgc     1008
Lys Ala Gly Pro Gly Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
            325                 330                 335

cca ccg tgc cca gca cct gaa ctc ctg ggg gga ccg tca gtc ttc ctc     1056
Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
        340                 345                 350

ttc ccc cca aaa ccc aag gac acc ctc atg atc tcc cgg acc cct gag     1104
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9

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Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
        355             360                 365

gtc aca tgc gtg gtg gtg gac gtg agc cac gaa gac cct gag gtc aag        1152
Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
        370             375                 380

ttc aac tgg tac gtg gac ggc gtg gag gtg cat aat gcc aag aca aag        1200
Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
385                 390                 395                 400

ccg cgg gag gag cag tac aac agc acg tac cgt gtg gtc agc gtc ctc        1248
Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
                405                 410                 415

acc gtc ctg cac cag gac tgg ctg aat ggc aag gag tac aag tgc aag        1296
Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
            420                 425                 430

gtc tcc aac aaa gcc ctc cca gcc ccc atc gag aaa acc atc tcc aaa        1344
Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
            435                 440                 445

gcc aaa ggg cag ccc cga gaa cca cag gtg tac acc ctg ccc cca tcc        1392
Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
    450                 455                 460

cgg gat gag ctg acc aag aac cag gtc agc ctg acc tgc ctg gtc aaa        1440
Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
465                 470                 475                 480

ggc ttc tat ccc agc gac atc gcc gtg gag tgg gag agc aat ggg cag        1488
Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
                485                 490                 495

ccg gag aac aac tac aag acc acg cct ccc gtg ctg gac tcc gac ggc        1536
Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
                500                 505                 510

tcc ttc ttc ctc tac agc aag ctc acc gtg gac aag agc agg tgg cag        1584
Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
        515                 520                 525

cag ggg aac gtc ttc tca tgc tcc gtg atg cat gag gct ctg cac aac        1632
Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
        530                 535                 540

cac tac acg cag aag agc ctc tcc ctg tct ccg ggt aaa tga              1674
His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
545                 550                 555


<210>   14
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<212>   PRT
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<220>
<223>   Flt1(1-3 deltaB)-Fc (Mut1)

<400>   14
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Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
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Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro
            20              25                  30          .

Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
        35              40                  45

Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
    50              55                  60

Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65              70              75                  80

Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
            85              90                  95

Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
        100             105                 110

Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
        115             120                 125

Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
    130             135             140

Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145             150             155                 160

Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
            165             170             175

Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
        180             185             190

Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
        195             200             205

Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
    210             215             220

Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val
225             230             235             240
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11

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Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr
            245             250                 255

Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Ile
            260             265                 270

Asp Gln Ser Asn Ser His Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile
        275             280                 285

Asp Lys Met Gln Asn Lys Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg
    290             295                 300

Ser Gly Pro Ser Phe Lys Ser Val Asn Thr Ser Val His Ile Tyr Asp
305             310                 315                 320

Lys Ala Gly Pro Gly Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
            325             330                 335

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
        340             345                 350

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
        355             360                 365

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
    370             375                 380

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
385             390                 395                 400

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
            405             410                 415

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
            420             425                 430

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
        435             440                 445

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
    450             455                 460

Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
465             470                 475                 480

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
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Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
            500   505   510

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
            515   520   525

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
        530   535   540

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
545   550   555

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<223>   Flt1(2-3 deltaB)-Fc(Mut2)

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<221>   CDS
<222>   (1)..(1359)

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Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
1   5   10   15

tgt ctg ctt ctc aca gga tct agt tcc gga ggt aga cct ttc gta gag   96
Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Gly Arg Pro Phe Val Glu
            20   25   30

atg tac agt gaa atc ccc gaa att ata cac atg act gaa gga agg gag   144
Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly Arg Glu
        35   40   45

ctc gtc att ccc tgc cgg gtt acg tca cct aac atc act gtt act tta   192
Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val Thr Leu
    50   55   60

aaa aag ttt cca ctt gac act ttg atc cct gat gga aaa cgc ata atc   240
Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg Ile Ile
65   70   75   80

tgg gac agt aga aag ggc ttc atc ata tca aat gca acg tac aaa gaa   288
Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys Glu
                85   90   95

ata ggg ctt ctg acc tgt gaa gca aca gtc aat ggg cat ttg tat aag   336
Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys
            100   105   110

aca aac tat ctc aca cat cga caa acc aat aca atc ata gat gtc caa   384
Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Val Gln

13

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ata agc aca cca cgc cca gtc aaa tta ctt aga ggc cat act ctt gtc          432
Ile Ser Thr Pro Arg Pro Val Lys Leu Leu Arg Gly His Thr Leu Val
    130                 135                 140

ctc aat tgt act gct acc act ccc ttg aac acg aga gtt caa atg acc          480
Leu Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr Arg Val Gln Met Thr
145                 150                 155                 160

tgg agt tac cct gat gaa att gac caa agc aat tcc cat gcc aac ata          528
Trp Ser Tyr Pro Asp Glu Ile Asp Gln Ser Asn Ser His Ala Asn Ile
                165                 170                 175

ttc tac agt gtt ctt act att gac aaa atg cag aac aaa gac aaa gga          576
Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys Asp Lys Gly
            180                 185                 190

ctt tat act tgt cgt gta agg agt gga cca tca ttc aaa tct gtt aac          624
Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys Ser Val Asn
        195                 200                 205

acc tca gtg cat ata tat gat aaa gca ggc ccg ggc gag ccc aaa tct          672
Thr Ser Val His Ile Tyr Asp Lys Ala Gly Pro Gly Glu Pro Lys Ser
    210                 215                 220

tgt gac aaa act cac aca tgc cca ccg tgc cca gca cct gaa ctc ctg          720
Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
225                 230                 235                 240

ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag gac acc ctc          768
Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255

atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg gac gtg agc          816
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
                260                 265                 270

cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac ggc gtg gag          864
His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285

gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac aac agc acg          912
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
    290                 295                 300

tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac tgg ctg aat          960
Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305                 310                 315                 320

ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc cca gcc ccc          1008
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
                325                 330                 335

atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga gaa cca cag          1056
Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350

gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag aac cag gtc          1104
Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
        355                 360                 365
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agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac atc gcc gtg      1152
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380

gag tgg gag agc aat ggg cag ccg gag aac aac tac aag acc acg cct      1200
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                     390                 395                 400

ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc aag ctc acc      1248
Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
                405                 410                 415

gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca tgc tcc gtg      1296
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
                420                 425                 430

atg cat gag gct ctg cac aac cac tac acg cag aag agc ctc tcc ctg      1344
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
            435                 440                 445

tct ccg ggt aaa tga                                                   1359
Ser Pro Gly Lys
        450


<210>   16
<211>   452
<212>   PRT
<213>   Artificial Sequence

<220>
<223>   Flt1(2-3 deltaB)-Fc

<400>   16

Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
1               5                   10                  15


Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Gly Arg Pro Phe Val Glu
            20                  25                  30


Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly Arg Glu
        35                  40                  45


Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val Thr Leu
    50                  55                  60


Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg Ile Ile
65                  70                  75                  80


Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys Glu
                85                  90                  95


Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys
```

15

Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Val Gln
      115   120   125

Ile Ser Thr Pro Arg Pro Val Lys Leu Leu Arg Gly His Thr Leu Val
      130   135   140

Leu Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr Arg Val Gln Met Thr
145   150   155   160

Trp Ser Tyr Pro Asp Glu Ile Asp Gln Ser Asn Ser His Ala Asn Ile
              165   170   175

Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys Asp Lys Gly
              180   185   190

Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys Ser Val Asn
              195   200   205

Thr Ser Val His Ile Tyr Asp Lys Ala Gly Pro Gly Glu Pro Lys Ser
      210   215   220

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
225   230   235   240

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
              245   250   255

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
              260   265   270

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
              275   280   285

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
      290   295   300

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
305   310   315   320

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
              325   330   335

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
              340   345   350

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Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
        355             360             365

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
        370             375             380

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385             390             395             400

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
            405             410             415

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
        420             425             430

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435             440             445

Ser Pro Gly Lys
    450


<210>  17
<211>  1389
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  Flt1(2-3)-Fc (Mut3)

<220>
<221>  CDS
<222>  (1)..(1389)

<400>  17
atg gtc agc tac tgg gac acc ggg gtc ctg ctg tgc gcg ctg ctc agc        48
Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
1               5               10              15

tgt ctg ctt ctc aca gga tct agt tcc gga ggt aga cct ttc gta gag        96
Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Gly Arg Pro Phe Val Glu
                20              25              30

atg tac agt gaa atc ccc gaa att ata cac atg act gaa gga agg gag        144
Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly Arg Glu
        35              40              45

ctc gtc att ccc tgc cgg gtt acg tca cct aac atc act gtt act tta        192
Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val Thr Leu
    50              55              60

aaa aag ttt cca ctt gac act ttg atc cct gat gga aaa cgc ata atc        240
Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg Ile Ile
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tgg gac agt aga aag ggc ttc atc ata tca aat gca acg tac aaa gaa    288
Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys Glu
                85              90              95

ata ggg ctt ctg acc tgt gaa gca aca gtc aat ggg cat ttg tat aag    336
Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys
            100             105             110

aca aac tat ctc aca cat cga caa acc aat aca atc ata gat gtc caa    384
Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Val Gln
            115             120             125

ata agc aca cca cgc cca gtc aaa tta ctt aga ggc cat act ctt gtc    432
Ile Ser Thr Pro Arg Pro Val Lys Leu Leu Arg Gly His Thr Leu Val
    130             135             140

ctc aat tgt act gct acc act ccc ttg aac acg aga gtt caa atg acc    480
Leu Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr Arg Val Gln Met Thr
145             150             155             160

tgg agt tac cct gat gaa aaa aat aag aga gct tcc gta agg cga cga    528
Trp Ser Tyr Pro Asp Glu Lys Asn Lys Arg Ala Ser Val Arg Arg Arg
                165             170             175

att gac caa agc aat tcc cat gcc aac ata ttc tac agt gtt ctt act    576
Ile Asp Gln Ser Asn Ser His Ala Asn Ile Phe Tyr Ser Val Leu Thr
                180             185             190

att gac aaa atg cag aac aaa gac aaa gga ctt tat act tgt cgt gta    624
Ile Asp Lys Met Gln Asn Lys Asp Lys Gly Leu Tyr Thr Cys Arg Val
            195             200             205

agg agt gga cca tca ttc aaa tct gtt aac acc tca gtg cat ata tat    672
Arg Ser Gly Pro Ser Phe Lys Ser Val Asn Thr Ser Val His Ile Tyr
    210             215             220

gat aaa gca ggc ccg ggc gag ccc aaa tct tgt gac aaa act cac aca    720
Asp Lys Ala Gly Pro Gly Glu Pro Lys Ser Cys Asp Lys Thr His Thr
225             230             235             240

tgc cca ccg tgc cca gca cct gaa ctc ctg ggg gga ccg tca gtc ttc    768
Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
                245             250             255

ctc ttc ccc cca aaa ccc aag gac acc ctc atg atc tcc cgg acc cct    816
Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
                260             265             270

gag gtc aca tgc gtg gtg gtg gac gtg agc cac gaa gac cct gag gtc    864
Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
            275             280             285

aag ttc aac tgg tac gtg gac ggc gtg gag gtg cat aat gcc aag aca    912
Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
    290             295             300

aag ccg cgg gag gag cag tac aac agc acg tac cgt gtg gtc agc gtc    960
Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
305             310             315             320
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ctc acc gtc ctg cac cag gac tgg ctg aat ggc aag gag tac aag tgc        1008
Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
            325                 330                 335

aag gtc tcc aac aaa gcc ctc cca gcc ccc atc gag aaa acc atc tcc        1056
Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
            340                 345                 350

aaa gcc aaa ggg cag ccc cga gaa cca cag gtg tac acc ctg ccc cca        1104
Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
            355                 360                 365

tcc cgg gat gag ctg acc aag aac cag gtc agc ctg acc tgc ctg gtc        1152
Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
        370                 375                 380

aaa ggc ttc tat ccc agc gac atc gcc gtg gag tgg gag agc aat ggg        1200
Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
385                 390                 395                 400

cag ccg gag aac aac tac aag acc acg cct ccc gtg ctg gac tcc gac        1248
Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
                405                 410                 415

ggc tcc ttc ttc ctc tac agc aag ctc acc gtg gac aag agc agg tgg        1296
Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
            420                 425                 430

cag cag ggg aac gtc ttc tca tgc tcc gtg atg cat gag gct ctg cac        1344
Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
            435                 440                 445

aac cac tac acg cag aag agc ctc tcc ctg tct ccg ggt aaa tga          1389
Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
        450                 455                 460


<210>   18
<211>   462
<212>   PRT
<213>   Artificial Sequence

<220>
<223>   Flt1(2-3)-Fc (Mut3)

<400>   18

Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
1               5                   10                  15


Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Gly Arg Pro Phe Val Glu
                20                  25                  30


Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly Arg Glu
            35                  40                  45


Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val Thr Leu
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19

Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg Ile Ile
65   70   75   80

Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys Glu
            85   90   95

Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys
            100   105   110

Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Val Gln
        115   120   125

Ile Ser Thr Pro Arg Pro Val Lys Leu Leu Arg Gly His Thr Leu Val
    130   135   140

Leu Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr Arg Val Gln Met Thr
145   150   155   160

Trp Ser Tyr Pro Asp Glu Lys Asn Lys Arg Ala Ser Val Arg Arg Arg
            165   170   175

Ile Asp Gln Ser Asn Ser His Ala Asn Ile Phe Tyr Ser Val Leu Thr
            180   185   190

Ile Asp Lys Met Gln Asn Lys Asp Lys Gly Leu Tyr Thr Cys Arg Val
        195   200   205

Arg Ser Gly Pro Ser Phe Lys Ser Val Asn Thr Ser Val His Ile Tyr
    210   215   220

Asp Lys Ala Gly Pro Gly Glu Pro Lys Ser Cys Asp Lys Thr His Thr
225   230   235   240

Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
            245   250   255

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
            260   265   270

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
        275   280   285

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
    290   295   300

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Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
305                 310             315                 320

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
                325             330                 335

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
            340             345             350

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
        355             360             365

Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
    370             375             380

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
385             390             395                 400

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
            405             410             415

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
        420             425             430

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
        435             440             445

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    450             455             460


<210>  19
<211>  1704
<212>  DNA
<213>  Artificial Sequence

<220>
<223>  Flt1(1-3 R->N) (Mut 4)

<220>
<221>  CDS
<222>  (1)..(1704)

<400>  19
atg gtc agc tac tgg gac acc ggg gtc ctg ctg tgc gcg ctg ctc agc      48
Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
1               5               10                  15

tgt ctg ctt ctc aca gga tct agt tca ggt tca aaa tta aaa gat cct      96
Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro
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gaa ctg agt tta aaa ggc acc cag cac atc atg caa gca ggc cag aca       144
Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
        35                  40                  45

ctg cat ctc caa tgc agg ggg gaa gca gcc cat aaa tgg tct ttg cct       192
Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
        50                  55                  60

gaa atg gtg agt aag gaa agc gaa agg ctg agc ata act aaa tct gcc       240
Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65                  70                  75                  80

tgt gga aga aat ggc aaa caa ttc tgc agt act tta acc ttg aac aca       288
Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
                85                  90                  95

gct caa gca aac cac act ggc ttc tac agc tgc aaa tat cta gct gta       336
Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
                100                 105                 110

cct act tca aag aag aag gaa aca gaa tct gca atc tat ata ttt att       384
Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
                115                 120                 125

agt gat aca ggt aga cct ttc gta gag atg tac agt gaa atc ccc gaa       432
Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
        130                 135                 140

att ata cac atg act gaa gga agg gag ctc gtc att ccc tgc cgg gtt       480
Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145                 150                 155                 160

acg tca cct aac atc act gtt act tta aaa aag ttt cca ctt gac act       528
Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
                165                 170                 175

ttg atc cct gat gga aaa cgc ata atc tgg gac agt aga aag ggc ttc       576
Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
                180                 185                 190

atc ata tca aat gca acg tac aaa gaa ata ggg ctt ctg acc tgt gaa       624
Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
                195                 200                 205

gca aca gtc aat ggg cat ttg tat aag aca aac tat ctc aca cat cga       672
Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
        210                 215                 220

caa acc aat aca atc ata gat gtc caa ata agc aca cca cgc cca gtc       720
Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val
225                 230                 235                 240

aaa tta ctt aga ggc cat act ctt gtc ctc aat tgt act gct acc act       768
Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr
                245                 250                 255

ccc ttg aac acg aga gtt caa atg acc tgg agt tac cct gat gaa aaa       816
Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys
        260                 265                 270
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22

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aat aag aac gct tcc gta agg cga cga att gac caa agc aat tcc cat          864
Asn Lys Asn Ala Ser Val Arg Arg Arg Ile Asp Gln Ser Asn Ser His
        275                 280                 285

gcc aac ata ttc tac agt gtt ctt act att gac aaa atg cag aac aaa          912
Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys
        290                 295                 300

gac aaa gga ctt tat act tgt cgt gta agg agt gga cca tca ttc aaa          960
Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys
305                 310                 315                 320

tct gtt aac acc tca gtg cat ata tat gat aaa gca ggc ccg ggc gag         1008
Ser Val Asn Thr Ser Val His Ile Tyr Asp Lys Ala Gly Pro Gly Glu
                325                 330                 335

ccc aaa tct tgt gac aaa act cac aca tgc cca ccg tgc cca gca cct         1056
Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
                340                 345                 350

gaa ctc ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa ccc aag         1104
Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
        355                 360                 365

gac acc ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg gtg gtg         1152
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
370                 375                 380

gac gtg agc cac gaa gac cct gag gtc aag ttc aac tgg tac gtg gac         1200
Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
385                 390                 395                 400

ggc gtg gag gtg cat aat gcc aag aca aag ccg cgg gag gag cag tac         1248
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
                405                 410                 415

aac agc acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac cag gac         1296
Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
                420                 425                 430

tgg ctg aat ggc aag gag tac aag tgc aag gtc tcc aac aaa gcc ctc         1344
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
        435                 440                 445

cca gcc ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag ccc cga         1392
Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
        450                 455                 460

gaa cca cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg acc aag         1440
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
465                 470                 475                 480

aac cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc agc gac         1488
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
                485                 490                 495

atc gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac tac aag         1536
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
                500                 505                 510
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23

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acc acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc tac agc        1584
Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
        515                 520                 525

aag ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc ttc tca        1632
Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
    530                 535                 540

tgc tcc gtg atg cat gag gct ctg cac aac cac tac acg cag aag agc        1680
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
545                 550                 555                 560

ctc tcc ctg tct ccg ggt aaa tga                                        1704
Leu Ser Leu Ser Pro Gly Lys
                565


<210>    20
<211>    567
<212>    PRT
<213>    Artificial Sequence

<220>
<223>    Flt1(1-3 R->N)-Fc (Mut4)

<400>    20

Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
1               5                   10                  15


Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro
            20                  25                  30


Glu Leu Ser Leu Lys Gly Thr Gln His Ile Met Gln Ala Gly Gln Thr
        35                  40                  45


Leu His Leu Gln Cys Arg Gly Glu Ala Ala His Lys Trp Ser Leu Pro
    50                  55                  60


Glu Met Val Ser Lys Glu Ser Glu Arg Leu Ser Ile Thr Lys Ser Ala
65                  70                  75                  80


Cys Gly Arg Asn Gly Lys Gln Phe Cys Ser Thr Leu Thr Leu Asn Thr
                85                  90                  95


Ala Gln Ala Asn His Thr Gly Phe Tyr Ser Cys Lys Tyr Leu Ala Val
                100                 105                 110


Pro Thr Ser Lys Lys Lys Glu Thr Glu Ser Ala Ile Tyr Ile Phe Ile
            115                 120                 125


Ser Asp Thr Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu
    130                 135                 140
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Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val
145             150             155             160

Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr
                165             170             175

Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe
            180             185             190

Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu
        195             200             205

Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg
    210             215             220

Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val
225             230             235             240

Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr
            245             250             255

Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys
            260             265             270

Asn Lys Asn Ala Ser Val Arg Arg Ile Asp Gln Ser Asn Ser His
        275             280             285

Ala Asn Ile Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys
    290             295             300

Asp Lys Gly Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys
305             310             315             320

Ser Val Asn Thr Ser Val His Ile Tyr Asp Lys Ala Gly Pro Gly Glu
                325             330             335

Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
            340             345             350

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
        355             360             365

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
    370             375             380
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25

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Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
385             390             395             400


Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
            405             410             415


Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
            420             425             430


Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
        435             440             445


Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
    450             455             460


Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
465             470             475             480


Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
            485             490             495


Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
        500             505             510


Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
        515             520             525


Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
    530             535             540


Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
545             550             555             560


Leu Ser Leu Ser Pro Gly Lys
            565


<210>   21
<211>   1453
<212>   DNA
<213>   Artificial Sequence

<220>
<223>   Flt1D2.Flk1D3.Fc$_{delta}$C1(a)Receptor

<220>
<221>   CDS
<222>   (69)..(1442)
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26

<400> 21
aagcttgggc tgcaggtcga tcgactctag aggatcgatc cccgggcgag ctcgaattcg   60

caaccacc atg gtc agc tac tgg gac acc ggg gtc ctg ctg tgc gcg ctg   110
         Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu
         1   5   10

ctc agc tgt ctg ctt ctc aca gga tct agt tcc gga ggt aga cct ttc   158
Leu Ser Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Gly Arg Pro Phe
15   20   25   30

gta gag atg tac agt gaa atc ccc gaa att ata cac atg act gaa gga   206
Val Glu Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly
                35   40   45

agg gag ctc gtc att ccc tgc cgg gtt acg tca cct aac atc act gtt   254
Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val
            50   55   60

act tta aaa aag ttt cca ctt gac act ttg atc cct gat gga aaa cgc   302
Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg
        65   70   75

ata atc tgg gac agt aga aag ggc ttc atc ata tca aat gca acg tac   350
Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr
        80   85   90

aaa gaa ata ggg ctt ctg acc tgt gaa gca aca gtc aat ggg cat ttg   398
Lys Glu Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu
95   100   105   110

tat aag aca aac tat ctc aca cat cga caa acc aat aca atc ata gat   446
Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp
                115   120   125

gtg gtt ctg agt ccg tct cat gga att gaa cta tct gtt gga gaa aag   494
Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu Lys
            130   135   140

ctt gtc tta aat tgt aca gca aga act gaa cta aat gtg ggg att gac   542
Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile Asp
        145   150   155

ttc aac tgg gaa tac cct tct tcg aag cat cag cat aag aaa ctt gta   590
Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu Val
        160   165   170

aac cga gac cta aaa acc cag tct ggg agt gag atg aag aaa ttt ttg   638
Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe Leu
175   180   185   190

agc acc tta act ata gat ggt gta acc cgg agt gac caa gga ttg tac   686
Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu Tyr
                195   200   205

acc tgt gca gca tcc agt ggg ctg atg acc aag aag aac agc aca ttt   734
Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr Phe
                210   215   220

gtc agg gtc cat gaa aag ggc ccg ggc gac aaa act cac aca tgc cca   782
Val Arg Val His Glu Lys Gly Pro Gly Asp Lys Thr His Thr Cys Pro

27

```
ccg tgc cca gca cct gaa ctc ctg ggg gga ccg tca gtc ttc ctc ttc      830
Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe
    240             245                 250

ccc cca aaa ccc aag gac acc ctc atg atc tcc cgg acc cct gag gtc      878
Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val
255             260                 265                 270

aca tgc gtg gtg gtg gac gtg agc cac gaa gac cct gag gtc aag ttc      926
Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
                275                 280                 285

aac tgg tac gtg gac ggc gtg gag gtg cat aat gcc aag aca aag ccg      974
Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
                290                 295                 300

cgg gag gag cag tac aac agc acg tac cgt gtg gtc agc gtc ctc acc     1022
Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
        305                 310                 315

gtc ctg cac cag gac tgg ctg aat ggc aag gag tac aag tgc aag gtc     1070
Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
    320                 325                 330

tcc aac aaa gcc ctc cca gcc ccc atc gag aaa acc atc tcc aaa gcc     1118
Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
335                 340                 345                 350

aaa ggg cag ccc cga gaa cca cag gtg tac acc ctg ccc cca tcc cgg     1166
Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg
                355                 360                 365

gat gag ctg acc aag aac cag gtc agc ctg acc tgc ctg gtc aaa ggc     1214
Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
        370                 375                 380

ttc tat ccc agc gac atc gcc gtg gag tgg gag agc aat ggg cag ccg     1262
Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
        385                 390                 395

gag aac aac tac aag acc acg cct ccc gtg ctg gac tcc gac ggc tcc     1310
Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
    400                 405                 410

ttc ttc ctc tat agc aag ctc acc gtg gac aag agc agg tgg cag cag     1358
Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
415                 420                 425                 430

ggg aac gtc ttc tca tgc tcc gtg atg cat gag gct ctg cac aac cac     1406
Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
                435                 440                 445

tac acg cag aag agc ctc tcc ctg tct ccg ggt aaa tgagcggccg c        1453
Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                450                 455
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<210> 22
<211> 458

<212> PRT
<213> Artificial Sequence

<220>
<223> Flt1D2.Flk1D3.Fc$_{delta}$C1(a) Receptor

<400> 22

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Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
1               5               10              15

Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Gly Arg Pro Phe Val Glu
            20              25              30

Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly Arg Glu
        35              40              45

Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val Thr Leu
    50              55              60

Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg Ile Ile
65              70              75              80

Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys Glu
            85              90              95

Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys
            100             105             110

Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Val Val
        115             120             125

Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu Lys Leu Val
    130             135             140

Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile Asp Phe Asn
145             150             155             160

Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu Val Asn Arg
            165             170             175

Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe Leu Ser Thr
            180             185             190

Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu Tyr Thr Cys
        195             200             205

Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr Phe Val Arg
```

Val His Glu Lys Gly Pro Gly Asp Lys Thr His Thr Cys Pro Pro Cys
225   230   235   240

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
                245   250   255

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
                260   265   270

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
            275   280   285

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
        290   295   300

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
305   310   315   320

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
                325   330   335

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
                340   345   350

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
                355   360   365

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
        370   375   380

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
385   390   395   400

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
                405   410   415

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
                420   425   430

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
            435   440   445

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    450   455

                                    30

<210> 23
<211> 1444
<212> DNA
<213> Artificial Sequence

<220>
<223> Flt1D2.VEGFR3D3.Fc$_{delta}$C1(a)Receptor

<220>
<221> CDS
<222> (69)..(1436)

<400> 23
aagcttgggc tgcaggtcga tcgactctag aggatcgatc cccgggcgag ctcgaattcg   60

caaccacc atg gtc agc tac tgg gac acc ggg gtc ctg ctg tgc gcg ctg   110
         Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu
           1   5   10

ctc agc tgt ctg ctt ctc aca gga tct agt tcc gga ggt aga cct ttc   158
Leu Ser Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Gly Arg Pro Phe
15   20   25   30

gta gag atg tac agt gaa atc ccc gaa att ata cac atg act gaa gga   206
Val Glu Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly
                35   40   45

agg gag ctc gtc att ccc tgc cgg gtt acg tca cct aac atc act gtt   254
Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val
            50   55   60

act tta aaa aag ttt cca ctt gac act ttg atc cct gat gga aaa cgc   302
Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg
            65   70   75

ata atc tgg gac agt aga aag ggc ttc atc ata tca aat gca acg tac   350
Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr
        80   85   90

aaa gaa ata ggg ctt ctg acc tgt gaa gca aca gtc aat ggg cat ttg   398
Lys Glu Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu
95   100   105   110

tat aag aca aac tat ctc aca cat cga caa acc aat aca atc ata gat   446
Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp
                115   120   125

atc cag ctg ttg ccc agg aag tcg ctg gag ctg ctg gta ggg gag aag   494
Ile Gln Leu Leu Pro Arg Lys Ser Leu Glu Leu Leu Val Gly Glu Lys
                130   135   140

ctg gtc ctc aac tgc acc gtg tgg gct gag ttt aac tca ggt gtc acc   542
Leu Val Leu Asn Cys Thr Val Trp Ala Glu Phe Asn Ser Gly Val Thr
            145   150   155

ttt gac tgg gac tac cca ggg aag cag gca gag cgg ggt aag tgg gtg   590
Phe Asp Trp Asp Tyr Pro Gly Lys Gln Ala Glu Arg Gly Lys Trp Val
    160   165   170

31

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ccc gag cga cgc tcc caa cag acc cac aca gaa ctc tcc agc atc ctg          638
Pro Glu Arg Arg Ser Gln Gln Thr His Thr Glu Leu Ser Ser Ile Leu
175                 180                 185                 190

acc atc cac aac gtc agc cag cac gac ctg ggc tcg tat gtg tgc aag          686
Thr Ile His Asn Val Ser Gln His Asp Leu Gly Ser Tyr Val Cys Lys
                    195                 200                 205

gcc aac aac ggc atc cag cga ttt cgg gag agc acc gag gtc att gtg          734
Ala Asn Asn Gly Ile Gln Arg Phe Arg Glu Ser Thr Glu Val Ile Val
                210                 215                 220

cat gaa aat ggc ccg ggc gac aaa act cac aca tgc cca ccg tgc cca          782
His Glu Asn Gly Pro Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro
            225                 230                 235

gca cct gaa ctc ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca aaa          830
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
        240                 245                 250

ccc aag gac acc ctc atg atc tcc cgg acc cct gag gtc aca tgc gtg          878
Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
255                 260                 265                 270

gtg gtg gac gtg agc cac gaa gac cct gag gtc aag ttc aac tgg tac          926
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
                275                 280                 285

gtg gac ggc gtg gag gtg cat aat gcc aag aca aag ccg cgg gag gag          974
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
                290                 295                 300

cag tac aac agc acg tac cgt gtg gtc agc gtc ctc acc gtc ctg cac         1022
Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
            305                 310                 315

cag gac tgg ctg aat ggc aag gag tac aag tgc aag gtc tcc aac aaa         1070
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
320                 325                 330

gcc ctc cca gcc ccc atc gag aaa acc atc tcc aaa gcc aaa ggg cag         1118
Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
335                 340                 345                 350

ccc cga gaa cca cag gtg tac acc ctg ccc cca tcc cgg gat gag ctg         1166
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
                355                 360                 365

acc aag aac cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat ccc         1214
Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
                370                 375                 380

agc gac atc gcc gtg gag tgg gag agc aat ggg cag ccg gag aac aac         1262
Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
                385                 390                 395

tac aag acc acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc ctc         1310
Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
400                 405                 410

tat agc aag ctc acc gtg gac aag agc agg tgg cag cag ggg aac gtc         1358
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32

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
415   420   .   425   430

ttc tca tgc tcc gtg atg cat gag gct ctg cac aac cac tac acg cag   1406
Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
                435   440   445

aag agc ctc tcc ctg tct ccg ggt aaa tga gcggccgc   1444
Lys Ser Leu Ser Leu Ser Pro Gly Lys
            450   455

<210>   24
<211>   455
<212>   PRT
<213>   Artificial Sequence

<220>
<223>   Flt1D2.VEGFR3D3.Fc_{delta}C1(a)Receptor

<400>   24

Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
1   5   10   15

Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Gly Arg Pro Phe Val Glu
                20   25   30

Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly Arg Glu
            35   40   45

Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val Thr Leu
        50   55   60

Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg Ile Ile
65   70   75   80

Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys Glu
                85   90   95

Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys
                100   105   110

Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Ile Gln
            115   120   125

Leu Leu Pro Arg Lys Ser Leu Glu Leu Leu Val Gly Glu Lys Leu Val
        130   135   140

Leu Asn Cys Thr Val Trp Ala Glu Phe Asn Ser Gly Val Thr Phe Asp
145   150   155   160

33

Trp Asp Tyr Pro Gly Lys Gln Ala Glu Arg Gly Lys Trp Val Pro Glu
                165   170   175

Arg Arg Ser Gln Gln Thr His Thr Glu Leu Ser Ser Ile Leu Thr Ile
                180   185   190

His Asn Val Ser Gln His Asp Leu Gly Ser Tyr Val Cys Lys Ala Asn
                195   200   205

Asn Gly Ile Gln Arg Phe Arg Glu Ser Thr Glu Val Ile Val His Glu
    210   215   220

Asn Gly Pro Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
225   230   235   240

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
                245   250   255

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
                260   265   270

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
                275   280   285

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
    290   295   300

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
305   310   315   320

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
                325   330   335

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
                340   345   350

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
                355   360   365

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
    370   375   380

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
385   390   395   400

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Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
            405                 410                 415


Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
            420                 425                 430


Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
            435                 440                 445


Leu Ser Leu Ser Pro Gly Lys
    450                 455



<210>   25
<211>   1377
<212>   DNA
<213>   Artificial Sequence

<220>
<223>   VEGFR1R2.Fc_{delta}C1(a) Receptor

<220>
<221>   CDS
<222>   (1)..(1377)

<400>   25
atg gtc agc tac tgg gac acc ggg gtc ctg ctg tgc gcg ctg ctc agc      48
Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
1               5                   10                  15

tgt ctg ctt ctc aca gga tct agt tcc gga agt gat acc ggt aga cct      96
Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Asp Thr Gly Arg Pro
            20                  25                  30

ttc gta gag atg tac agt gaa atc ccc gaa att ata cac atg act gaa     144
Phe Val Glu Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu
        35                  40                  45

gga agg gag ctc gtc att ccc tgc cgg gtt acg tca cct aac atc act     192
Gly Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr
    50                  55                  60

gtt act tta aaa aag ttt cca ctt gac act ttg atc cct gat gga aaa     240
Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys
65                  70                  75                  80

cgc ata atc tgg gac agt aga aag ggc ttc atc ata tca aat gca acg     288
Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr
                85                  90                  95

tac aaa gaa ata ggg ctt ctg acc tgt gaa gca aca gtc aat ggg cat     336
Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His
            100                 105                 110

ttg tat aag aca aac tat ctc aca cat cga caa acc aat aca atc ata     384
Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile
            115                 120                 125
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35

```
gat gtg gtt ctg agt ccg tct cat gga att gaa cta tct gtt gga gaa        432
Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu
    130             135              140

aag ctt gtc tta aat tgt aca gca aga act gaa cta aat gtg ggg att        480
Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile
145             150              155              160

gac ttc aac tgg gaa tac cct tct tcg aag cat cag cat aag aaa ctt        528
Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu
                165              170              175

gta aac cga gac cta aaa acc cag tct ggg agt gag atg aag aaa ttt        576
Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe
            180              185              190

ttg agc acc tta act ata gat ggt gta acc cgg agt gac caa gga ttg        624
Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu
        195              200              205

tac acc tgt gca gca tcc agt ggg ctg atg acc aag aag aac agc aca        672
Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr
    210              215              220

ttt gtc agg gtc cat gaa aag gac aaa act cac aca tgc cca ccg tgc        720
Phe Val Arg Val His Glu Lys Asp Lys Thr His Thr Cys Pro Pro Cys
225              230              235              240

cca gca cct gaa ctc ctg ggg gga ccg tca gtc ttc ctc ttc ccc cca        768
Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
                245              250              255

aaa ccc aag gac acc ctc atg atc tcc cgg acc cct gag gtc aca tgc        816
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
            260              265              270

gtg gtg gtg gac gtg agc cac gaa gac cct gag gtc aag ttc aac tgg        864
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
        275              280              285

tac gtg gac ggc gtg gag gtg cat aat gcc aag aca aag ccg cgg gag        912
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
    290              295              300

gag cag tac aac agc acg tac cgt gtg gtc agc gtc ctc acc gtc ctg        960
Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
305              310              315              320

cac cag gac tgg ctg aat ggc aag gag tac aag tgc aag gtc tcc aac       1008
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
                325              330              335

aaa gcc ctc cca gcc ccc atc gag aaa acc atc tcc aaa gcc aaa ggg       1056
Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
            340              345              350

cag ccc cga gaa cca cag gtg tac acc ctg ccc cca tcc cgg gat gag       1104
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
        355              360              365

ctg acc aag aac cag gtc agc ctg acc tgc ctg gtc aaa ggc ttc tat       1152
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Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
    370                 375             380

ccc agc gac atc gcc gtg gag tgg gag agc aat ggg cag ccg gag aac      1200
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
385                 390                 395                 400

aac tac aag acc acg cct ccc gtg ctg gac tcc gac ggc tcc ttc ttc      1248
Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
                405                 410                 415

ctc tac agc aag ctc acc gtg gac aag agc agg tgg cag cag ggg aac      1296
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
            420                 425                 430

gtc ttc tca tgc tcc gtg atg cat gag gct ctg cac aac cac tac acg      1344
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
        435                 440                 445

cag aag agc ctc tcc ctg tct ccg ggt aaa tga                          1377
Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    450                 455


<210>   26
<211>   458
<212>   PRT
<213>   Artificial Sequence

<220>
<223>   VEGFR1R2-Fc_delta_C1(a) Receptor

<400>   26

Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser
1               5               10              15


Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser Asp Thr Gly Arg Pro
            20              25              30


Phe Val Glu Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu
            35              40              45


Gly Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr
    50              55              60


Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys
65              70              75              80


Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr
                85              90              95


Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His
            100             105             110
```

37

Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile
        115   120   125

Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu
        130   135   140

Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile
145   150   155   160

Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu
                165   170   175

Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe
            180   185   190

Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu
        195   200   205

Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr
        210   215   220

Phe Val Arg Val His Glu Lys Asp Lys Thr His Thr Cys Pro Pro Cys
225   230   235   240

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
            245   250   255

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
            260   265   270

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
        275   280   285

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
        290   295   300

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
305   310   315   320

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
                325   330   335

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
            340   345   350

38

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu
         355   360   365

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
         370   375   380

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
385   390   395   400

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
             405   410   415

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
         420   425   430

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
         435   440   445

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    450   455

<210>   27
<211>   431
<212>   PRT
<213>   Artificial Sequence

<220>
<223>   Peptide

<400>   27

Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu Ile Ile His
1   5   10   15

Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro
             20   25   30

Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro
         35   40   45

Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser
    50   55   60

Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu Ala Thr Val
65   70   75   80

Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln Thr Asn
             85   90   95

Thr Ile Ile Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser
             100   105   110

Val Gly Glu Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn
         115   120   125

                                  39

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Val Gly Ile Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His
    130             135             140

Lys Lys Leu Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met
145             150             155             160

Lys Lys Phe Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp
                165             170             175

Gln Gly Leu Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys
            180             185             190

Asn Ser Thr Phe Val Arg Val His Glu Lys Gly Pro Gly Asp Lys Thr
        195             200             205

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
    210             215             220

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
225             230             235             240

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            245             250             255

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
            260             265             270

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
            275             280             285

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
    290             295             300

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
305             310             315             320

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            325             330             335

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Thr Cys Leu
            340             345             350

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
            355             360             365

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
    370             375             380

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
385             390             395             400

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
            405             410             415

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
            420             425             430
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